REMARKS

The following remarks and attached are submitted in response to the Communication dated July 14, 2004 with regard to the Request for Continued Prosecution of the instant application. In the Communication, the Examiner asserts that the request for continued examination was not fully responsive to the prior Office action because the claim listing in the amendment is incorrect, in that the response states that claim 22 is pending and the claim listing includes claim 22 as an "original" claim. Applicants submit herewith revised pages of the amendment filed March 3, 2004, particularly including page 2 providing the Status of the Claims as well as the Complete Listing of Claims in the Application.

Status of the Claims

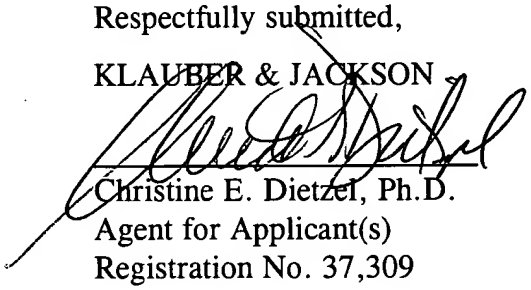
Claims 19-21, 24-27 and 29 are pending in the application.

CONCLUSION

Applicants respectfully request entry of the foregoing remarks and the attached corrected pages and claim listing in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated October 15, 2003.

Status of the Claims

Claims 19-21, 24-27 and 29 are pending in the application.

The §103 Rejections

Claims 19-21, 24 and 29 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Christensen et al [Am. J. Med. Genetics (5/21/1999) vol. 84 (2), pp. 151-157] in view of Steen et al [Prenatal Diagnosis (1998) vol. 18, pp.545-555]. In this new ground of rejection, the Examiner refers to prior remarks that Christensen et al teaches a method of estimating the susceptibility of a pregnant woman to have children with a neural tube defect (NTD) by analyzing nucleic acids and determining the presence of polymorphic alleles of MTHFR and MTR in both mothers and offspring, adding this dataset to a reference (control) dataset, formulates a model based on his combined datasets, and predicts the probability (odds ratio) for any woman to have children with NTDs based on the genetic data, with the Examiner further asserting that Christensen et al teaches measurement of two genetic variables, MTHFR and MTR, and thus suggests adding the MTR genetic variable to his MTHFR data. Steen, the Examiner states, teaches that both MTHFR mutation and vitamin B12 deficiency are independent risk factors for neural tube defects (NTD), wherein a correlation between an MTHFR mutation and spina bifida has been established, as has a correlation between reduced B12 and NTD, and further that the ratio of methionine to folate from maternal amniotic fluid may be indicative of NTD risk. Steen, it is asserted, concludes that both folate and vitamin B12 supplementation would be helpful in reducing the risk of NTD. The Examiner asserts that it would have been obvious to the skilled artisan at the time of the invention to have included the measurements and ratio calculations of Steen in the method of Christensen to genetically discriminate women at risk for having children with NTD. It is further asserted by

Complete Listing of Claims in Application U.S.S.N. 09/577,266

Claims 1-18 (cancelled)

19. (Previously amended) A method of estimating the susceptibility of an individual to have offspring that develop a developmental disorder comprising:

(a) collecting a biological sample from one or more participants; wherein a participant is either the individual or a blood relative of the individual; and wherein the biological sample contains nucleic acids and/or proteins of the participant;

(b) analyzing the nucleic acids and/or proteins from the biological sample; wherein said analyzing results in a partial or full genotype for the alleles of two or more genes involved in folate, pyridoxine, and/or cobalamin metabolism; and wherein said partial or full genotype forms a dataset of genetic explanatory variables for the participants;

(c) adding the datasets of genetic explanatory variables obtained from steps (a) and (b) to a genetic reference dataset therein forming a combined genetic dataset;

(d) formulating a model comprising the genetic explanatory variables obtained from the participants; and

(e) analyzing the combined genetic dataset by binary logistic regression;

wherein a predicted probability for the individual to have offspring that develop a developmental disorder is determined; and wherein the genetic and environmental susceptibility of an individual to have offspring that develop a developmental disorder is estimated, and wherein the individual is a pregnant woman.

20. (Original) The method of Claim 19 further comprising the step of :

(f) modifying the model by adding or subtracting a genetic explanatory variable; and re-analyzing the combined genetic dataset by binary logistic regression; wherein a model is chosen that best fits the data.

21. (Original) The method of Claim 20 further comprising the step of :

(g) testing the model for goodness of fit.

Claim 22 (cancelled)

Claim 23 (cancelled)

24. (Previously amended) A method of lowering the risk of a pregnant woman who has been determined by the method of Claim 21 to be susceptible to have offspring that develop a developmental disorder comprising administering methylfolate, cobalamin or pyridoxine to the pregnant woman, wherein said administering lowers the risk of the pregnant woman of giving birth to offspring with a developmental disorder.

25. (Previously amended) A method of determining if any treatment is advisable for a pregnant woman who has been determined by the method of Claim 21 to be susceptible to having offspring that develop a developmental disorder comprising determining the concentration of a risk factor from a tissue sample or body fluid from the pregnant woman; wherein when the concentration of the risk factor is statistically above or below an accepted normal range, treatment is advisable.

26. (Original) A method of monitoring the effect of the administration of methylfolate, cobalamin or pyridoxine to the pregnant woman of Claim 25, comprising determining the concentration of a risk factor from a tissue sample or body fluid from the pregnant woman; and wherein when the concentration of the risk factor is statistically within an accepted normal range, the treatment is effective.

27. (Original) The method of Claim 26 wherein the risk factor is selected from the group consisting of homocysteine, folate, and cobalamin.

Claim 28 (cancelled)

29. (Previously amended) A method of treating an asymptomatic individual determined by the method of Claim 21 to be susceptible to have offspring that develop a developmental disorder comprising administering methylfolate, cobalamin or pyridoxine.

Claims 30-47 (cancelled)